## Roles of ESCRT in autophagy-associated neurodegeneration.

**Journal:** Autophagy

**Publication Year:** 2008

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**PubMed link:** 18094607

**Funding Grants:** Gladstone CIRM Scholar Program

**Public Summary:**

**Scientific Abstract:**
Autophagy is a regulated pathway for bulk degradation of cytoplasmic contents and organelles, an important process involved in many physiological and pathological conditions in multiple organs, including the nervous system. It has been proposed that developing autophagosomes fuse with late endosomal compartments before their fusion with lysosomes; however, little is known about the functional relationship between the autophagy and endocytic pathways. In the endosomal-lysosomal pathway, a key step in sorting transmembrane cargo proteins is regulated by multimeric complexes called ESCRT (endosomal sorting complex required for transport). We recently reported that dysfunction of ESCRT-III, either by depletion of its essential subunit mSnf7-2 or by expression of a mutant CHMP2B protein associated with frontotemporal dementia linked to chromosome 3 (FTD3), caused autophagosome accumulation and dendritic retraction before neurodegeneration in cultured mature cortical neurons. This defect is likely a result of an abnormal fusion process between autophagosomes and endosomal compartments or lysosomes. This study suggests that defects in the late steps of the autophagy pathway may contribute to the pathogenesis of FTD and potentially other neurodegenerative diseases.